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| 10/824,833 | 04/14/2004 | Dennis A. Carson | 02307O-131710US | 7743 |

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

| EXAMINER | |
|---|---|
| OLSON, ERIC | |
| ART UNIT | PAPER NUMBER |
| 1623 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/824,833 | CARSON ET AL. | |
| | Examiner | Art Unit | |
| | Eric S. Olson | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *52-108* is/are pending in the application.

4a) Of the above claim(s) *52-63,83-111 and 114-118* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-82,112 and 113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## Detailed Action

This office action is a response to applicant's communication submitted December 20, 2006 wherein claims 1-51 are cancelled. This application claims benefit of provisional application 60/463152, filed April 14, 2003.

### *Election/Restrictions*

Applicant's provisional election with traverse of group VI, claims 64-82 and 112-113, drawn to a method of treating cancer by administering an IMBDH inhibitor in combination with an interferon inducer, filed December 20, 2006, is acknowledged. Applicant's arguments of record with respect to the aforementioned traversal are acknowledged and found to be not persuasive to remove the requirement for restriction. Applicant argues that groups V, VI, and VIII, using the same combination of therapeutic compounds, should be examined together. This argument is not persuasive because, although the different groups use the same therapeutic agents, they treat completely different disorders. Group VI is drawn to a method of treating cancer, which is very different from the viral infections treated by group V, the autoimmune disorders treated by group VII, and the skin disorders treated by group VIII. These different classes of disorders arise from completely different causes and are treated with different therapeutic agents. For example, most chemotherapeutic agents are not useful as antiviral compounds.

Applicant further argues that claim 64 is a genus claim linking treatments of melanoma. This argument is moot in view of the rejection of claim 64 as discussed below.

Finally, Applicant argues that examining groups IV, VI, and VIII together would not place an undue examination burden on the examiner. As discussed above, different disorders are discussed separately in the medical art, and will thus appear separately in the medical literature. As the claims are drawn to methods of treatment rather than pharmaceutical compositions, any search for the method of treatment will thus necessarily involve a search of the literature specific to the particular disease being treated. It should further be noted that the various disease categories of the different groups are already very broad and encompass a considerable amount of relevant literature. Therefore the search burden for examining the different groups together is judged to be undue.

For these reasons, the restriction requirement is deemed proper and made **FINAL**.

Applicant's election of a disease, interferon inducer and IMPDH inhibitor is acknowledged. However, the requirement for election of species is withdrawn. All claims will be examined with their full scope.

Claims 51-63, 83-111, and 114-118 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no

allowable generic or linking claim. Election was made **with** traverse in the reply filed on December 20, 2006.

Claims 64-82 and 112-113 are pending in this application and examined on the merits herein.

### *Claim Objections*

Claims 69-82 are objected to because of the following informalities: They depend from the cancelled claim 14, specifically by involving a nucleic acid of claim 14. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 69-82 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the nucleic acid of claim 14 being used in the claimed method.

Note that claim 14 has been cancelled and is also drawn to a non-elected invention. Insertion of the recitation of the nucleic acid of claim 14 into the method of claim 69 would be favorably considered.

In order to expedite prosecution, claims 69-82 will be examined inserting the recitation of the nucleic acid of claim 14 into claim 69, as has apparently been intended.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 64-66, 68-82 and 112-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a therapeutic method comprising administering specific inosine monophosphate dehydrogenase inhibitors such as mizoribine, mycophenolic acid, and ribivirin, does not reasonably provide enablement for any inosine monophosphate dehydrogenase inhibitor or for a prodrug of said compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method for treating a disorder by administering a chemical compound.

The state of the prior art: The Inosine monophosphate dehydrogenase inhibitors recited in instant claim 67 are known in the art and are recognized as having useful biological activities, particularly immunostimulation. Prodrugs of these compounds are not known in the art.

Various types of prodrugs exist in the prior art, which are used to produce different active agents *in vivo*. According to Silverman et al., (Reference included with PTO-892) prodrugs include esters, amides, schiff bases, oximes, acetals, enol esters, redox-activated protecting groups, polymer-bound drugs, bioprecursors, N- or O-alkylated drugs, azo compounds, sulfoxides, disulfides, phosphorylation substrates, and carboxylates, among others.

Furthermore, the prior art does not disclose the full range of all possible compounds that can inhibit inosine monophosphate dehydrogenase. Rather, there are likely a wide range of possible compounds having this activity that have not been contemplated by the prior art.

The relative skill of those in the art: The relative skill in the art is high.

The predictability or unpredictability of the art: As discussed above, there exist many different strategies by which one could attempt to generate a prodrug of a known compound. The appropriate prodrug for a particular application depends on various factors such as the compound being modified, the condition to be treated, the tissue to be affected, the species of the patient, and the desired rate of release. Because there

exist many different types of cancer and target tissues in which the cancer could occur, many different prodrug modifications must be considered to determine the optimal prodrug for each situation.

Furthermore, because the activation of a prodrug depends on its being metabolized *in vivo* by an enzyme, knowledge of the *in vivo* prodrug activity of a compound requires knowledge of the vast array of metabolic enzymes which are capable of acting on it. In order to know every possible prodrug of a compound, one must first know every enzyme which could potentially convert some other compound into that compound. Thus the design of prodrugs is complex and unpredictable.

In addition to the difficulties of developing prodrugs of known compounds, the pharmaceutical art is unpredictable in that it involves the interaction between diverse types of active agents and various complex biomolecules and biological pathways. It cannot be predicted, in the absence of experimental data, what biological activities if any will be possessed by a novel compound *in vivo*. In addition to the complex manner in which a compound will interact with its specific biological target (e.g. an enzyme or receptor) the bioavailability, metabolic transformation, toxicity, and interaction with other drugs for each compound must also be considered.

Furthermore, the art of organic synthesis is unpredictable in that there exists no routine, predictable method for synthesizing any arbitrarily chosen compound. Rather, one skilled in the art must undertake to develop a novel synthetic strategy for the synthesis of said novel compounds, in the process undertaking unpredictable experimentation.

The Breadth of the claims: The claimed invention encompasses a method comprising administering any compound that can inhibit inosine monophosphate dehydrogenase, regardless of the structure, or other physical or chemical properties of the compound. A prodrug encompasses and compound which is metabolized, in whole or in part, into an inosine monophosphate dehydrogenase inhibitor when administered to any living subject, whether plant, animal, or other.

The amount of direction or guidance presented: Applicant's specification defines the term "prodrug" on p. 26, lines 1-16 and furthermore suggests various prodrug modifications which could hypothetically be made to the claimed compounds. Applicant's specification does not actually give any guidance beyond this suggestion to try certain compounds.

The presence or absence of working examples: No working examples of prodrugs are provided.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as prodrug design. See MPEP 2164.

The quantity of experimentation necessary: One of ordinary skill in the art, in order to practice the claimed invention with the full range of prodrugs of compounds of formula I, would have to determine which compounds are in fact prodrugs of these active agents. For most derivatives of compounds of formula I, it is unknown whether they are or are not useful as prodrugs. Gathering this data for every compound fitting this description would involve *in vitro* screening of an large diversity of chemical

compounds for the desired enzymatic transformation, as well as *in vivo* testing of compound involving either human or animal subjects to determine therapeutic utility. *In vitro* testing requires that the compounds to be tested be synthesized and subjected to an appropriate screening method. Synthesis of diverse chemical structures requires novel and unpredictable experimentation in order to develop suitable synthetic methods. *In vivo* animal experiments include, along with induction of the disease state, administration of the potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, and disposal of dead animals after the protocol is finished. Human tests impose even greater ethical and regulatory burdens, as well as additional difficulty locating subjects. Because of the unpredictability of the art and the lack of comprehensive working examples covering any significant portion of the total number of potential prodrugs, these animal experiments would need to be repeated hundreds of times, and involve the maintenance, killing, dissection, and disposal of thousands of experimental animals, to establish the activity or lack thereof of every potential prodrug, thus presenting an a burden of undue experimentation to anyone practicing the invention with the full range of prodrugs claimed.

Similarly, one of ordinary skill in the art, in order to practice the claimed invention with the full range of IMPDH inhibitors beyond the meager number disclosed in the specification would be required to test potential compounds *in vivo* to determine whether a particular compound is useful as an IMPDH inhibitor. According to the 2006

Chemical Abstracts catalog, (Reference included with PTO-892) The Chemical Abstracts Registry contains entries for approximately 26 million compounds, all of which are potentially included in the claimed invention if they happen to have IMPDH inhibitory activity. For most compounds, it is unknown whether they are or are not useful as IMPDH inhibitors. Gathering this data for every compound known to man would involve *in vitro* screening of an enormous diversity of chemical compounds for IMPDH inhibitory activity, as well as *in vivo* testing of compounds having this activity involving either human or animal subjects to determine therapeutic utility. *In vitro* testing requires that the compounds to be tested be synthesized and subjected to an appropriate screening method. As described earlier, synthesis of diverse chemical structures requires novel and unpredictable experimentation in order to develop suitable synthetic methods. *In vivo* animal experiments include, along with induction of the disease state, administration of the potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, dissection of dead animals to collect data, and disposal of dead animals after the protocol is finished. Human tests impose even greater ethical and regulatory burdens, as well as additional difficulty locating subjects. Because of the unpredictability of the art and the lack of comprehensive working examples covering any significant portion of the total number of potential IMPDH inhibitors, these animal experiments would need to be repeated hundreds of times, and involve the maintenance, killing, dissection, and disposal of thousands of experimental animals, to establish the activity or lack thereof of every

possible IMPDH inhibitor, thus presenting an a burden of undue experimentation to anyone practicing the invention with the full range of IMPDH inhibitors claimed.

*Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."
Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the unpredictability of the art, Applicants fail to provide information sufficient to practice the claimed invention for all IMPDH inhibitors or prodrugs of IMPDH inhibitors.

Claims 64, 65, 67-82, and 112 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a leukemia, lymphoma, myeloma, melanoma, or renal cancer, does not reasonably provide enablement for a method of treating any cancer whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method for treating neoplastic disorders comprising administering an inosine monophosphate dehydrogenase inhibitor and an interferon inducer.

The state of the prior art: The skilled artisan would view cancer as a group of maladies not treatable with one medicament or therapeutic regimen. No single chemotherapeutic drug is useful for the treatment of every case of cancer. Indeed, some types of cancer to not respond well to any known chemotherapeutic drugs. According to the Merck Manual of Diagnosis and Therapy (Reference included with PTO-892), Hepatocellular carcinomas and renal cell carcinomas are not generally improved by chemotherapy. Acute lymphoblastic leukemia, on the other hand, responds well to a number of drugs, including vincristine, anthracyclines, and aspariginases, while acute mylogenous leukemia, on the other hand, responds to fewer drugs and is usually treated with cytarabine in combination with daunorubicin or idarubicin. Breast cancer is best treated with surgery and/or radiation, but the prognosis can be improved by the addition of adjuvant chemotherapy. Therefore the prior art does not recognize any universal treatment for cancer as a whole.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: As mentioned above, no single treatment is effective for all cancers. Different cancers vary widely in their response to different chemotherapy regimens. According to the Oxford Textbook of Oncology, (Reference cited in PTO-892) "The important criteria for the tumor include its sensitivity to cytostatic drugs, its clinical stage and its mass, the presence of measurable lesions or biochemical markers, and, finally, growth characteristics," as well as, "*In vitro* sensitivity tests have been disappointing. They predict well for resistance but are of little use for sensitivity," (p. 451, right column, second paragraph) and, "For many types of cancer the potential benefit of chemotherapy has not been demonstrated in well-designed clinical trials."

Based on the known teachings of the prior art such as that stated above, one skilled in the art would recognize that it is highly unpredictable in regard to the treatment in the instant case, including treating numerous and various tumors: gynecological tumors, ovarian carcinomas, testicle tumors, prostate carcinomas, skin cancer, kidney cancer, bladder tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, various types of leukemia and lymphomas, Hodgkin's disease, tumor illnesses of the CAN, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, especially intestine cancer, liver cancer, breast cancer, bronchial and lung carcinomas, melanomas, acute and chronic leukemias and benign papillomatosis tumors, by performing the necessary experimentation to develop an optimized dose-dense protocol for treating said cancers.

Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

The Breadth of the claims: The claimed method includes methods of treating any neoplastic disorder whatsoever, regardless of the location of the tumor, the type of tissue it arose from, the size or state of progression of the disease, and the presence or absence of drug-resistance phenotypes.

The amount of direction or guidance presented: Applicant's specification states that the claimed therapeutic methods are useful for treating cancer, and includes various *in vitro* demonstrations of the immunostimulatory properties of the claimed therapeutic method. However, the method is shown to be useful for treating viral and bacterial infections but is not demonstrated to possess anticancer activity.

The presence or absence of working examples: No working examples are provided of actual successful treatment of tumors *in vivo*.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the discovery of a novel chemotherapeutic agent. See MPEP 2164.

The quantity of experimentation necessary: In order to use the disclosed information to practice the claimed invention for a wide range of cancers using a wide range of drugs, a skilled practitioner of the art would develop a specific therapeutic regimen for each chemotherapy-responsive cancer. This would involve a process of

optimizing and testing various regimens *in vivo* for each type of cancer being treated. In particular, dose-response curves would need to be developed for a wide variety of different cancers, and it would need to be determined which cancers are or are not appropriately treated using the claimed agents. This process would involve unpredictable experimentation which would constitute an undue experimental burden on the practitioner.

*Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the unpredictability of the art, Applicants fail to provide information sufficient to practice the claimed invention for the treatment of all cancers.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tressler et al. (Reference included with PTO-892) in view of Hirahashi et al. (Reference included with PTO-892) Tressler et al. discloses a study of the anti-tumor activity of

mycophenolic acid and mycophenolate mofetil against various cancer cell lines including leukemia and lymphoma cell lines. (P. 568, left column, last paragraph – right column, first paragraph, third paragraph, p. 569, paragraphs 3-4) Mycophenolate mofetil is disclosed to be useful for delaying of reducing the growth of tumors *in vivo*. (p. 570, figures 1-3, p. 571, figures 4-5, p. 571, right column, second paragraph, p. 572, right column, paragraphs 1-2) Tressler et al. does not disclose a method further comprising administering an interferon inducer.

Hirahashi et al. discloses that administration of a hot water extract of the cyanobacterium *Spirulina platensis* is an effective anti-cancer agent *in vivo*. (p. 423, left column, first paragraph – p. 424, left column, second paragraph) Administration of spirulina is shown to induce greater IFN-gamma production in response to interleukin 12 and interleukin 18. (pp. 426-428, figures 1-3) Thus the spirulina extract is an interferon inducer that is also useful for treating cancer.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer the mycophenolate mofetil of Tressler et al. in combination with the spirulina extract of Hirahashi et al. to a patient suffering from cancer. One of ordinary skill in the art would have been motivated to combine the references because both therapeutic methods are disclosed to be useful for treating the same condition, namely cancer. One of ordinary skill in the art would have reasonably expected success because both therapies are disclosed to be useful individually.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albrecht et al. (Foreign Patent DE19811313, Reference included with PTO-892, translation included with PTO-892) in view of Hirahashi et al. (Reference included with PTO-892) Albrecht et al. discloses a procedure for determining the enzymatic activity of inosine monophosphate dehydrogenase in a patient being treated with an IMPDH inhibitor. (P. 1, lines 3-6) These inhibitors are revealed to be clinically useful for treating diseases including cancer. (p. 1, lines 31-34, p. 7, lines 49-57) IMPDH inhibitors that can be used clinically and monitored by the disclosed method include Mycophenolate mofetil, mycophenolic acid, Tiazofurin, Ribavirin, and mizorbine. (p. 7, lines 49-57) Albrecht et al. does not disclose a method further comprising administering an interferon inducer.

Hirahashi et al. discloses that administration of a hot water extract of the cyanobacterium *Spirulina platensis* is an effective anti-cancer agent *in vivo*. (p. 423, left column, first paragraph – p. 424, left column, second paragraph) Administration of spirulina is shown to induce greater IFN-gamma production in response to interleukin 12 and interleukin 18. (pp. 426-428, figures 1-3) Thus the spirulina extract is an interferon inducer that is also useful for treating cancer.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer the IMPDH inhibitors of Albrecht et al. in combination with the spirulina extract of Hirahashi et al. to a patient suffering from cancer. One of ordinary skill in the art would have been motivated to combine the references because both therapeutic methods are disclosed to be useful for treating the same condition, namely

cancer. One of ordinary skill in the art would have reasonably expected success because both therapies are disclosed to be useful individually.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 68, 112, and 113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albrecht et al. (Foreign Patent DE19811313, Reference included with PTO-892, translation included with PTO-892) in view of Hirahashi et al. (Reference included with PTO-892) further in view of Kirkwood et al. (Reference included with PTO-892) The disclosure of Albrecht et al. in view of Hirahashi et al. is discussed above. Albrecht et al. in view of Hirahashi et al. does not disclose a method further comprising administering exogenous type I interferon.

Kirkwood et al. reviews various studies of the antitumor effects of interferons, particularly interferon-$\alpha$. (a type I interferon) Results are summarized in tale I, pp. 339-341. Results for specific tumors are also disclosed including renal cell carcinoma, (p. 344) melanoma (p. 345) lymphoma (p. 346) myeloma (p. 347) and leukemia. (p. 348)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Albrecht et al. in view of Hirahashi et al. by further administering exogenous type I interferon. One of ordinary skill in the art would have been motivated to add the interferon because Kirkwood et al. gives multiple examples of type I interferon being useful for treating various cancers. One of ordinary skill in the art would have reasonably expected success because both therapies are disclosed to be useful individually.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 69-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tressler et al. (Reference included with PTO-892) in view of Hirahashi et al. (Reference included with PTO-892) further in view of Krug et al. (Reference included with PTO-892) The disclosure of Tressler et al. in view of Hirahashi et al. is discussed above. Tressler et al. in view of Hirahashi et al. does not disclose a method comprising administering an interferon inducer that is an oligonucleotide.

Krug et al. discloses a study of the interferon-inducing activities of CpG oligonucleotides. (p. 2155, left column, third paragraph) Several CpG ODNs are disclosed as having IFN-alpha and IFN-beta stimulating activities in PBMC cells, (p. 2155, right column, figure 1)

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute IFN-stimulating CpG oligonucleotides of the types disclosed by Krug et al. in place of the spirulina extract in the method of Tressler et al. in view of Hirahashi et al. discussed above. One of ordinary skill in the art would have been motivated to modify the invention in this manner because the CpG oligonucleotides produce the same biological effect, stimulating interferon production, as the spirulina extract. One of ordinary skill in the art would reasonably have expected success because Hirahashi et al. already discloses an interferon inducer that is useful for treating cancer.

Thus the invention taken as a whole is *prima facie* obvious.

## Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson
Patent Examiner
AU 1623
3/12/07

Anna Jiang
3/15/07
Supervisory Patent Examiner
AU 1623